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10/533,157	12/07/2005	Jean-Jacques Bourguignon		5191

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EXAMINER	
KIFLE, BRUCK	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/533,157	BOURGUIGNON ET AL.	
	Examiner	Art Unit	
	Bruck Kifle	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claim Rejections - 35 USC § 112

Claims 29-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

These claims require "at least one phosphodiesterase 2 inhibitor." The claims do not require that the compound possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of compounds that is defined by novelty.

A chemical compound can be a pharmaceutical composition, a protein, a peptide, a non-peptide compound, an animal tissue extract, nucleic acids, sugars, antisense molecules, peptidomimetic, transformed cells, radiation, antibodies, antibody fragments, cyclic peptides, agonists, antagonists, inhibitors, enhancers, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as proteinaceous substances, known, and unknown compounds.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not

described. Accordingly, the specification does not provide adequate written description of the claimed genus.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003) and *University of Rochester v. G.D. Searle & Co. et al.* CAFC [(03-1304) 13 February 2004]. In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting prostaglandin synthesis in a human host using an unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35 U.S.C. §112, since the patent described the compound's desired function of reducing activity of the enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since the invention consists of performing "assays" to screen compounds in

order to discover those with the desired effect. The patent did not name even one compound that assays would identify as suitable for practice of the invention, or provide information such that one skilled in art could identify a suitable compound. And since the specification did not indicate that compounds are available in public depository, the claimed treatment method cannot be practiced without the compound. Thus the inventors cannot be said to have "possessed" the claimed invention without knowing of a compound or method certain to produce said compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406." Applicants have made no

assertion that there is any correlation between the biological function of the compound being claimed and its structure.

According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement,

"The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In *re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

This case was filed before Applicants had a clear idea of the structures of their desired compounds, how to make their compounds and how to use them.

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The

description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

In *Fiers v. Sugano*, 25 USPQ2d 1601, U.S. Court of Appeals Federal Circuit repeated its views concerning the propriety of defining a chemical by its function and emphasized that for all chemicals including DNA "Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived." They further required the inventor to have a "mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property."

Both *Fiers v. Sugano*, 25 USPQ2d 1601 and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 were quoted with approval by the U.S. Court of Appeals Federal Circuit in *Burroughs Wellcome Co. v. Barr Laboratories Inc.,* 32 USPQ2d 1915 who added, "An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. ... The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention."

Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

Claims 36-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A complete prior art search could not be conducted for these claims because of the numerous problems with the claims. These are listed below.

i) The term "general" in claim 36, renders the claims indefinite because one cannot say what else is intended besides the structural formula and definition of the variables. Deletion is suggested.

ii) The group "(C_5-C_{18}) heterocycle" or "(C_5-C_{12}) heterocycle" is indefinite because a heterocycle necessarily requires the presence of a hetero atom and cannot be made up of solely carbon atoms. The kind of heteroatoms and number of rings intended is also not known.

iii) In the definition of R_5 as naphthyl, the phrase "when R_5 is a naphthyl group substituted in position 6, then the latter is not attached to the rest of the molecule in position 2" is unclear. The "latter" would be the substituent and this is not attached to anything. Appropriate correction is required.

iv) Also in the definition of R_5, which is defined as "when R5 represents a phenyl group substituted at least in position 3, said substituent being selected in the group consisting of: an alkyl, halogenoalkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, heterocycle, heterocycloalkyl group, a OH, =O, NO2, NH2, CN, CF3, COR', COOR', (C1-C6)alkoxy, (di)(C1-C6)alkylamino, NHCOR', CONR'R" group, in which R' and R" are such as defined hereinabove, CHO, CONH2,

phenyl optionally substituted, in particular by an acetyl group, by a halogen atom (Cl), by a CONH2 group or by a CN, prop-l-ynyl optionally substituted, in particular by a benzyloxy or tert-butyl carbamate, hex-l-ynyl optionally substituted, in particular by a CN or NH2, pentyl optionally substituted, in particular by a CONH2, hexyl, piperidinyl group optionally substituted, in particular by a prop-l-ynyl, benzylaminomethyl, acetamide (CH3CONH), aminomethyl, NH2CS-, 4-phenyl-1, 3-thiazol-2-yl, -CONHBenzyl, -COOEthyl, -CONHiPropyl, -CONH-(CH2)n-CONH2 (n representing a whole number from 1 to 6), -CONR'R" group, with R' and R", which are the same or different, representing a C1-C6 alkyl group or a hydrogen atom, -(4-benzylpyperazin-l-yl)carbonyl, -CONH-(CH2)n- phenyl (n representing a whole number from 1 to 6), imidazolyl, piperazinyl optionally substituted, in particular by a phenyl group," have several problems that have been underlined for Applicants convenience.

The term "being" should be replaced by "is" in the second line of the definition.

The term "heterocycle" is indefinite because it is not known how many atoms make up the ring, which atoms are present and what kind of a ring (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.) is intended. Similarly, the term "heterocycloalkyl" is indefinite because of the same reason and because it is unclear whether this is a heterocycle or cycloalkyl. A clarification is required.

The groups "optionally substituted" render the claims indefinite because one skilled in the art cannot say which substituents are intended and which are not. The phrase "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Following "halogen" in parenthesis "Cl" is present. This is indefinite because one cannot say what is intended. Are all halogens intended or is only chloro intended?

The group acetamide is further defined as "(CH3CONH)." This is not necessary. One definition is sufficient.

The term "representing" should be replaced by "represents."

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 36 recites the broad recitation "heterocycle", and the claim also recites "imidazolyl" and "piperazinyl" which are the narrower statement of the range/limitation.

iv) The last paragraph on page 8 reads "the alkyl, cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, phenyl, naphthyl, heterocycle, heterocycloalkyl group or the hydrocarbon chain defined hereinabove being optionally substituted by one or more substituents, which are the same or different, preferably selected in the group consisting of a halogen atom, an alkyl, halogenoalkyl,

cycloalkyl, alkenyl, alkynyl, aralkyl, aryl, heterocycle, heterocycloalkyl group, a OH, =O, NO2, NH2, CN, CF3, COR', COOR', (C1-C6)alkoxy, (di)(C1-Cs)alkylamino, NHCOR' and CONR'R" group, in which R' and R" are such as defined hereinabove, the substituents also being optionally substituted." Similar to the point above there are ranges within ranges (aryl and phenyl, naphthyl), indefinite terms, "preferably" and substituents which are not defined (the substituents also being optionally substituted). Appropriate correction is required.

v) Regarding claim 43, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 50-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating the diseases recited.

The claims read on treating pathologies involving the central nervous system, in particular due to a deregulation of the function of a neurotransmitter or to a deficiency in the release of a neurotransmitter, by administering to a subject in need of such treatment at least one compound such as defined in claim 36 (claim 50), a method according to claim 50, wherein the pathology is selected in the group consisting of depression, schizophrenia, anxiety, bipolar disorder, attention deficit disorders, sleep disorders, obsessive compulsive disorder, fibromyalgia, Tourette's syndrome, pharmacodependence, epilepsy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, obesity and Lewy body dementia; A method for treating pathologies involving the peripheral nervous system and peripheral organs in general, in particular pathologies of the type reduced natriuria,

acute renal failure, hepatic dysfunction, acute hepatic failure, in particular due to age, and pathologies due to or involving dysfunctions of prolactin secretion, such as restless legs syndrome, rheumatismal, allergic or auto-inflammatory disorders, such as rheumatoid arthritis, rhinitis and asthma, by administering to a subject in need of such treatment a compound such as defined in claim 36 (claim 52); A method for treating disorders of the central or peripheral nervous system, of chronic or acute nature, by administering to a subject in need of such treatment a compound such as defined in claim 36 (claim 53) and A method for treating memory impairment or cognitive impairment, in particular mild cognitive impairment, for treating neurodegenerative diseases, or for treating obesity, by administering to a subject in need of such treatment a compound such as defined in claim 36.

The how to use portion of the statute has not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what disease and what symptoms are to be treated.

Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' compounds falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in

terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates."

Applicants have not demonstrated nor have they alleged there is any correlation between the *in vitro* assays they disclose in Tables 1 and 2 and clinical efficacy against any disease. Case law is clear on this point. In an unpredictable art, such as CNS disease therapy, *in vitro* assays may be used for enablement only if there is a well-established correlation between the assay and clinical efficacy.

The claims are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating depression, schizophrenia, anxiety, bipolar disorder, attention deficit disorders, sleep disorders, obsessive compulsive disorder, fibromyalgia, Tourette's syndrome, pharmacodependence, epilepsy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, obesity and Lewy body dementia, pathologies involving the peripheral nervous system and peripheral organs in general, pathologies of the type reduced natriuria, acute renal failure, hepatic dysfunction, acute hepatic failure, in particular due to age, and pathologies due to or involving dysfunctions of prolactin secretion, such as restless legs syndrome, rheumatismal, allergic or auto-inflammatory disorders, such as rheumatoid arthritis, rhinitis and asthma; a method for treating disorders of the central or peripheral nervous system, of chronic or acute nature; a method for treating memory impairment or cognitive impairment, in particular mild cognitive impairment, for treating neurodegenerative diseases, or for treating obesity.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The how to use requirement of the enablement statute, when applied to method claim, refers to operability and how to make the claimed method work "The factors to be considered (in making an enablement rejection) have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. The issue is the correlation between clinical efficacy for treating all of theses diseases and Applicants' in vitro PDE2 inhibitor assay.

a) Determining if any particular claimed compound would treat the diseases recited, would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials with a number of fundamentally different diseases listed above, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large degree of experimentation.

b) The direction concerning treating these diseases found in the specification merely states Applicants' intention to do so. Since no PDE2 inhibitor has ever been used to treat all of these diseases, how is the skilled physician to know what dose to use for each of these different diseases? Applicants do no assert and it is not art-recognized that this in vitro assay is correlated to clinical efficacy of the diseases objected to.

c) There is no working example of treatment of any rejected disease in man or animals.

d) The nature of the invention is clinical treatment of disease with PDE2 inhibitors, which involves physiological activity.

e) The state of the clinical arts in the PDE2 related diseases is extensive with no single report of success for treating the diseases objected to.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience.

g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ l8, 24 (CCPA 1970).

h) The scope of the claims involves all of the thousands of compounds as well as the hundreds of diseases embraced by the claims. Thus, the scope of the claim is very broad. The scope of uses embraced by these claims is not remotely enabled based solely on instant compounds ability to inhibit PDE2.

There are many neurotransmitters which have different effects, such as, Acetylcholine (ACh), dopamine, norepinephrine, serotonin, histamine, epinephrine, GABA, glycine, glutamate, aspartate and peptides, such as, bradykinin, substance P, vasopressin, etc.

Many neurotransmitters vary in how they affect the body and its functions. Some examples of neurotransmitter action:

Acetylcholine - voluntary movement of the muscles

Norepinephrine - wakefulness or arousal

Dopamine - voluntary movement and motivation, "wanting"

Serotonin - memory, emotions, wakefulness, sleep and temperature regulation

GABA (gamma aminobutyric acid) - inhibition of motor neurons

Glycine - spinal reflexes and motor behaviour

Neuromodulators - sensory transmission-especially pain.

The notion that one can treat pathologies due to a deregulation of the function of a neurotransmitter or to a deficiency in the release of a neurotransmitter generally, is absolutely contrary to what is known about neurotransmitters.

MPEP 2164.0l(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

There are compounds excluded by proviso. If these compounds are excluded to avoid prior art rejections, Applicants are urgently requested to point to these compounds in the prior art because the disclosure of these excluded compounds is material to the examination of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

> such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beton (GB 1,346,176). The reference teaches a generic group of 1,4-benzodiazepinones which embraces applicants' claimed compounds (See page 1). The claims differ from the reference by reciting specific species and a more limited genus than the reference. However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

The closest prior art compounds are those of examples 1 and 2. These close prior art compounds differ from the claimed compounds by being ring position isomers at instant phenyl at R_5. The claims require the substituent to e at the three position over the two position of the prior art compound. Position isomers are well established as being prima facie structurally obvious. See: Ex parte Engelhardt, 208 USPQ 343, 349; In re Mehta, 146 USPQ 284; In re Surrey, 138 USPQ 67; Ex parte Ullyot 103 USPQ 185; Ex parte Naito 168 USPQ 437, 439; In re Norris 84 USPQ 459; Ex parte Allais 152 USPQ 66; Ex parte Henkel 130 USPQ 474; Ex parte

Biel 124 USPQ 109; In re Crownse 150 USPQ 554; In re Fouche 169 USPQ 431; Ex parte Ruddy 121 USPQ 427; In re Wiechert 152 USPQ 249.

For example "Position Isomerism has been used as a tool to obtain new and useful drugs" (Engelhardt), and "Position isomerism is a fact of close structural similarity" (Mehta, emphasis in the original).

Homologues, different halogen and ring position isomers of the excluded compounds are embraced by the claims. Should the excluded compounds be found in the prior art, their disclosure would render the instant claims obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is 571-272-0668. The examiner can normally be reached on Mondays-Fridays from 8:30 AM -6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruck Kifle/
Primary Examiner
Art Unit 1624

November 5, 2007